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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,281	12/12/2005	Kazutaka Tachibana	TACHIBANA1	3438

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EXAMINER	
CHENG, KAREN	
ART UNIT	PAPER NUMBER
1626	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,281	TACHIBANA ET AL.	
	Examiner	Art Unit	
	Karen Cheng	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10* is/are rejected.

7)☒ Claim(s) *6 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/12/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-13 are pending in the instant application.

Priority

The application is a 371 of International Application No. PCT/JP04/08211, filed on 6/11/2004, which claims the benefit of foreign priority under 35 U.S.C. 119, to Japanese Application No. 2003-168267, filed on 06/12/2003. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on 06/12/2003. It is noted, however, that applicant has not provided an English translation of the document as required by 35 U.S.C. 119(b).

Information Disclosure Statement

Applicant's Information Disclosure Statement filed on 12/12/05 has been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

Claim Objections

Claims 6 and 8 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 7. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Note: The recitation of the intended use of the claimed compounds does not further limit the scope of the claimed composition/drug. Additionally, the specification discloses the claimed compounds to be anti-androgen agents, and claims that recite inherent properties of compounds do not further limit the scope of the claim. If claim 8 is amended to reflect a method of use,

it would still fail to comply with the enablement rejection as discussed below. It is suggested that applicant cancel claims 6 and 8.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 10 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131,149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

The nature of the invention

The nature of the invention is directed to the use of a compound of claim 1 as a anti-androgen agent that is used for the treatment or prevention of prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis. An anti-androgen agent is defined as an androgen receptor antagonist on p. 1 of the specification.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat or prevent diseases such as prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes

that that contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any preventive regimen on its fact.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The burden of enabling one skilled in the art to prevent a disease would be much greater than that of enabling the treatment of such a disease. In the instant case, the specification does not provide guidance as to how one skilled in the art would accomplish the objective of treating or preventing prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active ingredients for prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis.

Specifically, it is highly unlikely, and the Office would require experimental evidence to support the contention that the claim specified could actually treat or prevent prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis by simply administering, by any method, a therapeutically active amount of the claim specified agents. The specification fails to enable one of ordinary skill in the art to practice the presently

claimed method for prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis.

"To prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Webster's II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compositions can be administered to order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of subjects who have the potential of becoming afflicted with prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis in general. Since applicants "preventive" assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. Applicants have not provided any competent evidence or disclosed test results that are highly predictive for the pharmaceutical use of preventing any disease. Hence, one of skill in the art is unable to fully predict possible preventive results from the administration of the claimed compound due to the absence of convincing evidence that said composition has an effect on any disease.

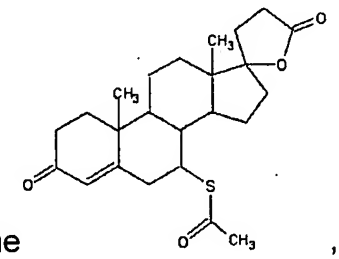
Applicants' claims also include the treatment of prostate cancer. The state of the prior art is that cancer therapy remains highly unpredictable. The treatment options for prostate cancer depend largely on whether the tumor has spread. Treatment options include radiation therapy, surgery, or watchful waiting. Tumors that grow beyond the edge of the prostate may be treated with hormones. According to Isaacs et al, the treatment of patients with metastatic prostate cancer with drugs that block production of

androgen (ie. anti-androgens) rarely cures the cancer. The initial positive response is almost always followed by an unresponsive, hormone-refractory stage. As a result, cells may become supersensitive to androgen, causing antiandrogens to promote androgen function rather promoting the intended inhibitory effect (p. 26). Thus, there exists a high level of unpredictability in the art, especially in regards to treatment protocol of prostrate cancer using anti-androgens.

According to http://www.nlm.nih.gov/medlineplus/ency/article/000381.htm, benign prostatic hypertrophy (BPH) is treated by surgery, watchful waiting, lifestyle changes and medication. Only three classes of drugs are listed: inasteride, alpha 1-blockers, and antibiotics. No indication of the effect of anti-androgens is given and hence the unpredictability of anti-androgens in treating BPH is high.

In regards to male pattern baldness, it is known that individuals that have the genetic deficiency of 5α-reductase experience male pattern hair loss. Treatment can include the utility of 5α-reductase inhibitors that target dihydrotestosterone (DHT) (Olsen et al, p. 301). Only two drugs, finasteride and minoxidil, are FDA-approved for treatment of male pattern hair loss, which illustrates the difficulty in finding a drug that targets DHT. Furthermore, there is no indication that the compounds described in the specification are 5α-reductase inhibitors; instead they are described as having anti-androgen activity.

Sexual precociousness, otherwise known as precocious puberty can be divided into 2 distinct categories, which are gonadotropin-dependent precocious puberty and gonadotropin-independent precocious puberty. Treatment often depends on the

underlying etiology of the precocious pseudopuberty. An example of an antiandrogen, spironolactone  , used in treatment of precocious puberty has a chemically different core than the instantly claimed invention (Fenton et al).

In regards to common acne, seborrhea and hypertrichosis, no test results or indication of the effectiveness of the compounds on the effect of skin flaking is given. Applicant has not provided evidence that use of anti-androgens would have any effect on these conditions. Moreover, there are no test results indicating that any of the claimed compounds have an effect on these conditions, either *in vitro* or *in vivo* (ie animal test results).

The amount of direction or guidance present and the presence or absence of working examples

The specification states that there is an expectation that the compounds will act as anti-androgen agents (p. 70). However, no indication of the effect of the compound in living organisms (*in vivo*) is given. Additionally there are no tests performed on subjects that show signs of prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis. Given the complexity of the diseases claimed by the applicants, different methods of treatment used to treat these diseases, and lack of apparent examples in the current literature that resemble applicant's instant invention, the level of unpredictability in the art is high.

The breadth of the claims

The instant breadth of the rejected claims is broader than the disclosure, specifically, the instant claims include the treatment and prevention of prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis but does not specify who/what is being treated. The specification only provides evidence for the inhibitory effect the compounds have on a androgen receptors. However no test results disclosing the actual effect of the compounds on subjects that show evidence of any of these diseases has been shown.

The quantity or experimentation needed and the level of skill in the art

It would require undue experimentation of one of ordinary skill in the art to ascertain the effectiveness of the compound in the treatment and prevention of prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis. Factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention and unpredictability of treating and preventing prostate cancer, benign prostatic hypertrophy, male pattern baldness, sexual precociousness, common acne, seborrhea and hypertrichosis, and the lack of working examples regarding the activity as claimed, one skilled in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in cope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, it is apparent that undue experimentation is necessary because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Therefore, claims 8-9 are rejected under 35 U.S.C. § 112, 1st paragraph.

Claim Rejections - 35 USC § 112 – 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 provides for the use of compounds of the formula I, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Conclusion

A search was made of the prior art, and the closest art was found in European Publication No. EP0580459 whereby a similar compound that has an aryl sulfonylalkyl

[–$(CH_2)_nSO_2$-Ar] substituent rather than aminosulfonylalkyl substituent from the imidazoline core is disclosed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cheng whose telephone number is 571-272-6233. The examiner can normally be reached on M-F, 9AM to 5:30PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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